

## **I. AMENDMENT**

### **Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

### **Listing of Claims:**

1. (currently amended) A method for creating a nucleic acid comprising the steps of:
  - (a) annealing a defined primer nucleic acid to at least one first single stranded template nucleic acid,
  - (b) performing a first extension by extending the primer nucleic acid employing the first template nucleic acid to form an extended nucleic acid,
  - (c) denaturing the extended nucleic acid from the first template nucleic acid,
  - (d) annealing the extended nucleic acid to at least a second single stranded template nucleic acid whose sequence is not identical to the first template nucleic acid,
  - (e) performing a second extension by extending the extended nucleic acid employing the second template nucleic acid to form a twice extended nucleic acid,
  - (f) adding ~~at least one chain terminating agent comprising~~ at least one dideoxynucleotide, a dideoxynucleotide analog or a dideoxynucleotide derivative before or during at least one of the first extension or the second extension, wherein said ~~chain terminating agent~~dideoxynucleotide, a dideoxynucleotide analog or a dideoxynucleotide derivative is incorporated into said extended nucleic acid, and

- (g) modifying or removing the ~~chain-terminating agent~~ dideoxynucleotide, dideoxynucleotide analog or dideoxynucleotide derivative from the extended nucleic acid, if a further extension is to be performed.
2. (previously presented) The method of claim 1, further comprising:
- (a) denaturing the twice extended nucleic acid from the second template nucleic acid
  - (b) annealing the twice extended nucleic acid to a third template nucleic acid, and
  - (c) performing a third extension by extending the twice extended nucleic acid employing the third template nucleic acid to form a thrice extended nucleic acid.
3. (currently amended) The method of claim 2, further comprising adding ~~least one chain-terminating agent comprising~~ at least one dideoxynucleotide, a dideoxynucleotide analog or a dideoxynucleotide derivative before or during the third extension.
4. (previously presented) The method of claim 2, further comprising at least one additional series of denaturing from a template, annealing to a further template, and performing of extension.
5. (previously presented) The method of claim 4, further defined as comprising between one and about five hundred additional series of denaturing from a template, annealing to a further template, and performing of extension.
6. (currently amended) The method of claim 2, further comprising adding ~~least one chain-terminating agent comprising~~ at least one dideoxynucleotide, a dideoxynucleotide analog or a dideoxynucleotide derivative before or during each extension.

7. (currently amended) The method of claim 2, wherein at least one extension is performed without the addition of a ~~chain-terminating agent~~dideoxynucleotide, a dideoxynucleotide analog or a dideoxynucleotide derivative.

8. (canceled)

9. (currently amended) A method for creating a nucleic acid comprising the steps of:

(a) annealing a defined first primer nucleic acid to at least one first single stranded template nucleic acid,

(b) performing a first extension by extending the first primer nucleic acid employing the first template nucleic acid to form a first extended nucleic acid

(c) denaturing the first extended nucleic acid from the first template nucleic acid,

(d) annealing the first extended nucleic acid to at least a second single stranded template nucleic acid whose sequence is not identical to the first template nucleic acid, and

(e) performing a second extension by extending the extended nucleic acid employing the second template nucleic acid to form a twice extended nucleic acid,

(f) adding at least one ~~chain-terminating agent~~dideoxynucleotide, a dideoxynucleotide analog or a dideoxynucleotide derivative before or during at least one of the first extension or the second extension, and

(g) modifying or removing the ~~chain-terminating agent~~dideoxynucleotide, dideoxynucleotide analog or dideoxynucleotide derivative from the extended nucleic acid, if a further extension is to be performed.

10. (canceled)
11. (currently amended) The method of claim 9, wherein said ~~chain-terminating agent~~ dideoxynucleotide, dideoxynucleotide analog or dideoxynucleotide derivative is incorporated into said first or second extended nucleic acid.
12. The method of claim 9, further comprising:
- (a) denaturing the twice extended nucleic acid from the second template nucleic acid
  - (b) annealing the twice extended nucleic acid to a third template nucleic acid, and
  - (c) performing a third extension by extending the twice extended nucleic acid employing the third template nucleic acid to form a thrice extended nucleic acid.
13. (currently amended) The method of claim 12, further comprising adding at least one ~~chain-terminating agent~~ dideoxynucleotide, a dideoxynucleotide analog or a dideoxynucleotide derivative before or during the third extension.
14. (previously presented) The method of claim 12, further comprising at least one additional series of denaturing from a template, annealing to a further template, and performing of extension.
15. (previously presented) The method of claim 14, further defined as comprising between one and five hundred additional series of denaturing from a template, annealing to a further template, and performing of extension.
16. (currently amended) The method of claim 12, further comprising adding at least one ~~chain-terminating agent~~ dideoxynucleotide, a dideoxynucleotide analog or a dideoxynucleotide derivative present before or during each extension.

17. (currently amended) The method of claim 12, wherein at least one extension is performed without the addition of a ~~chain-terminating agent~~ dideoxynucleotide, a dideoxynucleotide analog or a dideoxynucleotide derivative.

18. (currently amended) The method of claim 9, wherein said ~~chain-terminating agent~~ dideoxynucleotide, a dideoxynucleotide analog or a dideoxynucleotide derivative is removed by at least one exonuclease.

19. (previously presented) The method of claim 9, wherein said first single stranded template nucleic acid or said second single stranded template nucleic acid vary in size, sequence, resistance to cleavage or resistance to exonuclease degradation.

20. (canceled)

21. (previously presented) The method of claim 9, wherein said method produces a plurality of extended nucleic acids.

22. (previously presented) The method of claim 21, wherein said plurality of extended nucleic acids comprises an extension ladder.

23. (previously presented) The method of claim 21, wherein said plurality of extended nucleic acids vary in length, sequence, resistance to cleavage or resistance to exonuclease degradation.

24. (previously presented) The method of claim 23, wherein said plurality of extended nucleic acids comprises nucleic acids of different sequence.

25. (previously presented) The method of claim 24, wherein said different sequence varies by one nucleotide.

26. (previously presented) The method of claim 23, wherein said plurality of extended nucleic acids comprise different lengths.
27. (previously presented) The method of claim 26, wherein said different lengths comprise one nucleotide increments.
28. (previously presented) The method of claim 27, wherein said different lengths comprise more than one nucleotide increments.
29. (previously presented) The method of claim 9, wherein the extended nucleic acid comprises at least one partly double stranded nucleic acid or at least one fully double stranded nucleic acid.
30. (previously presented) The method of claim 9, wherein said at least one first primer nucleic acid comprises a sequence designed to anneal to a specific sequence comprising said first or second template nucleic acid.
31. (previously presented) The method of claim 9, wherein said at least one first primer nucleic acid is resistant to cleavage or exonuclease digestion.
32. (previously presented) The method of claim 9, wherein said defined first primer nucleic acid is a plurality of primers.
33. (previously presented) The method of claim 32, wherein said plurality of primers vary in length, sequence, resistance to cleavage or resistance to exonuclease degradation.
34. (previously presented) The method of claim 9, wherein the first extended nucleic acid comprises the primer nucleic acid.
35. (previously presented) The method of claim 9, wherein said first or second extended nucleic acid is a recombinant, mutagenized or chimeric nucleic acid.

36. (previously presented) The method of claim 9, wherein said at least one first single stranded template nucleic acid or said at least one second single stranded template nucleic acid is a plurality of template nucleic acids.
37. (previously presented) The method of claim 9, further comprising the addition of at least one length-altering agent.
38. (previously presented) The method of claim 37, wherein the length-altering agent comprises a nucleotide, a nucleotide derivative, a nucleotide analog, a chemical treatment or a combination thereof.
39. (previously presented) The method of claim 38, wherein said length-altering agent comprises a nucleotide incorporated into said first or second extended nucleic acid.
40. (previously presented) The method of claim 39, wherein said nucleotide comprises at least one ribonucleotide.
41. (previously presented) The method of claim 40, wherein said length-altering agent further comprises treatment with an alkaline condition or a ribonuclease.
42. (previously presented) The method of claim 40, wherein said length-altering agent further comprises treatment with alkaline phosphatase and an exonuclease.
43. (previously presented) The method of claim 38, wherein said length-altering agent comprises a nucleotide derivative incorporated into said extended nucleic acid.
44. (previously presented) The method of claim 38, wherein the length-altering agent comprises a nucleotide analog incorporated into said extended nucleic acid.

45. (previously presented) The method of claim 44, wherein said nucleotide analog comprises at least one  $\alpha$ -phosphorothioate nucleotide.
46. (previously presented) The method of claim 45, wherein said length-altering agent further comprises alkylation of said extended nucleic acid.
47. (previously presented) The method of claim 38, wherein the length-altering agent comprises a chemical treatment of said extended nucleic acid.
48. (previously presented) The method of claim 47, wherein said chemical treatment is a Maxam and Gilbert treatment or variant thereof.
49. (previously presented) A nucleic acid produced by the method of claim 9.
50. (previously presented) A proteinaceous composition encoded by a nucleic acid produced by the process of claim 9.
51. (previously presented) The proteinaceous composition of claim 50, wherein said proteinaceous composition comprises an enzyme.
52. (previously presented) The proteinaceous composition of claim 50, wherein said proteinaceous composition comprises a protein, a polypeptide or a peptide.
53. (previously presented) A method for creating a nucleic acid comprising the steps of:
- (a) annealing a defined primer nucleic acid to at least one first single stranded template nucleic acid,
  - (b) performing a first extension by extending the primer nucleic acid employing the first template nucleic acid to form an extended nucleic acid,



- (c) denaturing the extended nucleic acid from the first template nucleic acid,
- (d) annealing the extended nucleic acid to at least a second single stranded template nucleic acid whose sequence is not identical to the first template nucleic acid,
- (e) performing a second extension by extending the extended nucleic acid employing the second template nucleic acid to form a twice extended nucleic acid,
- (f) adding at least one length-altering agent before or during at least one of the first extension or the second extension, and
- (g) modifying or removing the length-altering agent from the extended nucleic acid, if a further extension is to be performed.

54. (previously presented) The method of claim 53, wherein said length-altering agent comprises at least one ribonucleotide incorporated into said first or second extended nucleic acid.

55. (previously presented) The method of claim 53, wherein said length-altering agent comprises at least one nucleotide analog incorporated into said first or second extended nucleic acid followed by alkylation of said extended nucleic acid.

56. (previously presented) The method of claim 53, wherein said length-altering agent comprises at least one Maxam and Gilbert treatment or variant thereof.

57. (previously presented) The method of claim 53, wherein said length-altering agent is at least one chain-terminating agent, wherein said chain-terminating agent comprises at least one dideoxynucleotide, a dideoxynucleotide analog or a dideoxynucleotide derivative incorporated into said extended nucleic acid.

## **II. RESPONSE TO OFFICE ACTION**

### **A. Status of the Claims**

Claims 1-7, 9-19, and 21-57 are pending in this application. Claims 1, 3, 6, 7, 9, 11, 13, and 16-18 have been amended to more particularly claim the invention. Support for the amendments may be found throughout the specification. Claim 10 has been canceled.

### **B. The Rejections Under 35 U.S.C. § 112, Second Paragraph, Are Overcome**

Claims 7, 17, 34, 37-48, and 53-57 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that the applicant regards as the invention. Applicants respectfully traverse.

Claims 7 and 17 stand rejected on the grounds that it is not clear whether a chain-terminating agent is added. The Action appears to be based on a reading of claims 7 and 17 that requires the method as a whole to be performed without the addition of any chain-terminating agent. This is not the case. Claims 7 and 17 do not eliminate step f) from claims 1 and 9, respectively. Rather, claims 7 and 17 provide that “at least one extension is performed without the addition of a chain-terminating agent.” This language is consistent with step f) of claims 1 and 9 where a chain-terminating agent is added “during at least one of the first extension or the second extension.”

The Action rejects claim 34 on the grounds that this claim is not further limiting from claim 9 because the first extended nucleic acid of claim 9 would necessarily comprise the primer. Applicants respectfully traverse. Claim 34 is narrowing because the first extended nucleic acid of claim 9 may or may not comprise the primer nucleic acid. Applicants direct the Examiner’s attention to the specification at page 33, lines 21 to 23. Here the specification provides that the primer sequence may or may not comprise the extended nucleic acid because in some

embodiments the primer may be degraded or removed by cleavage. Consequently, claim 34 is further limiting of claim 9.

Finally, the Action rejects claims 37-48 and 53-57 on the grounds that the recitation “length-altering agent” is not defined in the specification. Applicants respectfully traverse. The recitation “length-altering agent” is defined in the specification as “an agent that may either terminate chain-elongation or be used to later shorten an extended nucleic acid” (p. 34, ln. 19-21). In addition, as noted by the Examiner, numerous examples of length-altering agents can be found in the specification (see e.g., p. 7-9, 13-15, 34-35). The claims, therefore, set out and circumscribe the subject matter with a reasonable degree of clarity and particularity such that a person of ordinary skill in the art would be apprised of their scope.

In view of the foregoing, the applicants respectfully request the reconsideration and withdrawal of the rejections to claims 7, 17, 34, 37-48, and 53-57 under 35 U.S.C. § 112, second paragraph.

**C. The Rejections Under 35 U.S.C. § 102 Are Overcome**

***1. Claims 7 and 17 Are Not Anticipated by Arnold et al.***

Claims 7 and 17 stand rejected under § 102(e) as anticipated by Arnold *et al.* (US Patent 6,153,410). The Action argues that the claims are directed to an *in vitro* recombination method using a defined primer, and not adding any chain-terminating agents. Applicants respectfully traverse.

As described above with regard to the rejection of claims 7 and 17 under 35 U.S.C. § 112, second paragraph, claims 7 and 17 do not require the method as whole to be performed without the addition of any chain-terminating agent. Rather, claims 7 and 17 provide that “at least one extension is performed without the addition of a chain-terminating agent.” This

language is consistent with step f) of claims 1 and 9 where a chain-terminating agent is added “during at least one of the first extension or the second extension.” The claims, therefore, are not directed to an *in vitro* recombination method using a defined primer, and not adding any chain-terminating agents. Therefore, Arnold *et al.* does not anticipate claims 7 and 17. Applicants respectfully request the reconsideration and withdrawal of this rejection.

**2. *Claims 1-7, 9-17, 19, 21-39, 43-44, 46, 48-53, and 55-57 Are Not Anticipated by Short***

Claims 1-7, 9-17, 19, 21-39, 43-44, 46, 48-53, and 55-57 stand rejected under § 102(b) as anticipated by Short (WO 98/01581). Applicants respectfully traverse.

Short appears to teach a method that it refers to as DNA “shuffling” or alternatively, “Sexual PCR” (Short, p. 8, ln. 25-26). This method appears to involve obtaining a pool of polynucleotides and subjecting the pooled nucleotides to random primer extension. The extension process may be blocked or interrupted using adducts to create a population of shorter polynucleotides with widely varying 5’ and 3’ ends. The population of shorter polynucleotides can then be “shuffled” by denaturing and then annealing in the presence of a polymerase without primers (*see e.g.*, Short p. 65, example 3). Alternatively, oligonucleotides that comprise areas of identity and heterology may be added to the population of random extension products. The pool of polynucleotides and oligonucleotides are denatured and then allowed to anneal in the presence of a polymerase, thus forming a double-stranded polynucleotide.

**a. *The Short Reference Does Not Teach Defined Primers***

To anticipate a claim, the reference must teach every element of the claim (MPEP § 2131). Short does not teach every element of the applicants’ claimed invention. In particular, Short does not teach the use of defined primers.

Short specifically teaches random primers, and all of its examples appear to be based on random primers. At best, Short teaches primers generically. The disclosure of a genus does not anticipate a species. MPEP § 2131.02. Consequently, teaching “primers” does not anticipate “defined primers.” To the extent that alleged unexpressed inherent characteristics form the basis of an anticipation rejection, it is noted by Applicants that these characteristics must necessarily flow from the disclosure. *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991) (“To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.”).

The Short reference is silent with regard to “defined primers,” and the Action has not presented evidence that makes it clear that the missing descriptive matter is necessarily present in the reference. Rather, the Action improperly infers that Short teaches non-random primer extension. “Even assuming that Short teaches random primer extension in his first step, he clearly teach [sic] non-random primer extension when the added polynucleotides anneal to the resultant polynucleotides. That is, the added polynucleotides act as defined primers, as they anneal to specific resultant polynucleotides.” Paper Number 14, p. 6-7. From this statement, it appears that the Action is defining the primers in terms of the template, *i.e.*, the extension products. Applicants respectfully submit that the Action has mischaracterized the extension products and, consequently, mischaracterized the primers.

Short appears to teach random primer extension in its first step. The obvious result of random primer extension is the generation of a population of random extension products. The

Action, however, characterizes these random extension products as “specific resultant polynucleotides.” Paper Number 14, p. 7. By Short’s own definition, the products of random primer extension are not “specific polynucleotides” because the end points are not certain. Short at p. 19, ln. 18-19. The Action has not provided any evidence to support the position that oligonucleotides that anneal to a population of random extension products act as defined primers merely by virtue of their ability to anneal.

***b. The Short Reference Does Not Teach Adding At Least One Chain-Terminating Agent, Wherein the Chain-Terminating Agent is Incorporated Into the Extended Nucleic Acid***

Short does not teach adding at least one chain-terminating agent before or during at least one of the first or second extension, wherein said chain-terminating agent is incorporated into said extended nucleic acid. However, in the interest of advancing the prosecution, applicants have amended claims 1, 3, 6, 7, 9, 11, 13, and 16-18 to remove the recitation “chain-terminating agent.” The amended claims read on adding at least one dideoxynucleotide, dideoxynucleotide analog, or dideoxynucleotide derivative before or during at least one of the first extension or second extension, wherein said dideoxynucleotide, dideoxynucleotide analog, or dideoxynucleotide derivative is enzymatically incorporated into said extended nucleic acid. Short does not teach a dideoxynucleotide, dideoxynucleotide analog, or dideoxynucleotide derivative that is enzymatically incorporated into the extended nucleic acid. Short defines the recitation “means for slowing or halting the PCR amplification process” on page 25. This definition does not include dideoxynucleotides, dideoxynucleotide analogs, or dideoxynucleotide derivatives. Neither does Short teach agents that are incorporated enzymatically; nor does it teach agents that are incorporated only into the extension products (i.e., not into the template).

*c. Conclusion*

To anticipate a claim, the reference must teach every element of the claim (MPEP § 2131). For the reasons described above, Short does not teach each and every element set forth in the claims. The Action has thus clearly failed to meet the burden under 35 U.S.C. §102. Applicants respectfully request the reconsideration and withdrawal of the rejection.

**D. The Rejection Under 35 U.S.C. § 103(a) is Overcome**

***1. Claims 18, 45, and 47-48 Are Not Unpatentable in View of Short and Rosenthal et al.***

Claims 18, 45, and 47-48 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Short (WO 98/01581) in view of Rosenthal *et al.* (US Patent 6,087,095). Applicants respectfully traverse.

To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. MPEP § 2143.03, citing *In re Royka*, 490 F.2d 981 (CCPA 1074). As discussed above, Short does not teach all the claim limitations of claims 1-7, 9-17, 19, 21-39, 43-44, 46, 48-53, and 55-57, and therefore it cannot form the basis of the rejection of dependent claims 18, 45, and 47-48 as argued by the Action.

First, Short does not teach the limitation of defined primers. Short appears to teach random primer extension. The reference is silent with regard to “defined primers,” and the Action has not presented evidence that makes it clear that the missing descriptive matter is necessarily present in the reference. Even if it is assumed that Short teaches primers generically, the disclosure of a genus does not anticipate a species. MPEP § 2131.02.

Second, Short does not teach adding at least one dideoxynucleotide, dideoxynucleotide analog, or dideoxynucleotide derivative before or during at least one of the first extension or second extension, wherein said dideoxynucleotide, dideoxynucleotide analog, or

dideoxynucleotide derivative is enzymatically incorporated into said extended nucleic acid. Short appears to teach only the use of UV light and DNA adducts to slow or halt the extension process. Short, p. 25. This does not include dideoxynucleotides, dideoxynucleotide analogs, or dideoxynucleotide derivatives. Neither does it include agents that are incorporated enzymatically nor agents that are incorporated only into the extension products (*i.e.*, not into the template). Because Short does not teach all of these limitations, it cannot anticipate claims 1-7, 9-17, 19, 21-39, 43-44, 46, 48-53, and 55-57. Consequently, viewing Short in light of Rosenthal *et al.* cannot obviate claims 18, 45, and 47-48, which depend from claim 9.

In addition, there must be some motivation or suggestion to combine the references, which is not present in this case. MPEP § 2143. In fact, Rosenthal *et al.* teaches away from the presently claimed invention. The Rosenthal *et al.* reference does not provide for the annealing of an extension product made upon a first template to a second template that is not of the identical sequence as the first. The goal and purpose of the Rosenthal *et al.* methods is to create readable sequence data from a single template. The presence of more than one template wherein the templates are not of identical sequence would only confound the expected results, and therefore Rosenthal *et al.* can only teach away from the combination as claimed. That a reference teaches away is sufficient on its own to defeat a *prima facie* case of obviousness, even if all the elements of the invention are shown to be available in the art. *Winner Int'l. Royalty Corp. v. Wang*, 202 F.3d 1340, 1349-50 (Fed. Cir. 2000).

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection.



**2. Claims 40-42 and 54 Are Not Unpatentable in View of Short and Laney et al.**

Claims 40-42 and 54 stand rejected under § 103(a) as unpatentable over Short (WO 98/01581) in view of Laney *et al.* (US Patent 5,679,512). Applicants respectfully traverse.

To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. MPEP § 2143.03, citing *In re Royka*, 490 F.2d 981 (CCPA 1074). As discussed above, Short does not teach all the claim limitations of claims 1-7, 9-17, 19, 21-39, 43-44, 46, 48-53, and 55-57, and therefore it cannot form the basis of the rejection of dependent claims 40-42 and 54 as argued by the Action.

First, Short does not teach the limitation of defined primers. Short appears to teach random primer extension. The reference is silent with regard to “defined primers,” and the Action has not presented evidence that makes it clear that the missing descriptive matter is necessarily present in the reference. Even if it is assumed that Short teaches primers generically, the disclosure of a genus does not anticipate a species. MPEP § 2131.02.

Second, Short does not teach adding at least one dideoxynucleotide, dideoxynucleotide analog, or dideoxynucleotide derivative before or during at least one of the first extension or second extension, wherein said dideoxynucleotide, dideoxynucleotide analog, or dideoxynucleotide derivative is enzymatically incorporated into said extended nucleic acid. Short appears to teach only the use of UV light and DNA adducts to slow or halt the extension process. Short, p. 25. This does not include dideoxynucleotides, dideoxynucleotide analogs, or dideoxynucleotide derivatives. Neither does it include agents that are incorporated enzymatically nor agents that are incorporated only into the extension products (*i.e.*, not into the template). Because Short does not teach all of these limitations, it cannot anticipate claims 1-7,

9-17, 19, 21-39, 43-44, 46, 48-53, and 55-57. Consequently, viewing Short in light of Laney *et al.* cannot obviate claims 40-42 and 54, which depend from claims 9 and 53.

In addition, there must be some motivation or suggestion to combine the references. MPEP § 2143. Laney *et al.* appears to teach polynucleotide primers comprising modified nucleotides at the 3' end of the primer. It does not appear to teach incorporating modified nucleotides at any other position in the extension product. The Action states that "in view of the teachings of Laney, it would have been obvious to one of skill in the art at the time of the invention was made to have modified the methods of Recombinant Catalysts and Rosenthal so as to have included the steps of incorporating modified bases into the 3' end of a polynucleotide primer, in order to have achieved the benefits of amplifying a plurality of alternative templates." Paper 14, p. 8-9. Applicants submit that incorporating modified bases into the 3' end of a polynucleotide primer would either block primer extension completely or permit the primer to be cleaved from the extension product. It would not, however, achieve "the benefits of amplifying a plurality of alternative templates" as suggested by the Action. Therefore, it would not have been obvious to one of skill in the art at the time of the invention was made to have modified the methods of Short in view of Laney *et al.*

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection.

**E. Summary**

In light of the preceding remarks, the applicants respectfully submit that all claims are in condition for allowance, and an early indication to that effect is earnestly solicited. Should Examiner Spiegler have any questions regarding this response, please contact the undersigned at the telephone number listed below.